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**Core transcriptional regulatory circuit controlled by the TAL1 complex in human T cell acute lymphoblastic leukemia.**

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**Public Summary:**

The oncogenic transcription factor TAL1/SCL is aberrantly expressed in over 40% of cases of human T cell acute lymphoblastic leukemia (T-ALL), emphasizing its importance in the molecular pathogenesis of T-ALL. Here we identify the core transcriptional regulatory circuit controlled by TAL1 and its regulatory partners HEB, E2A, LMO1/2, GATA3, and RUNX1. We show that TAL1 forms a positive interconnected autoregulatory loop with GATA3 and RUNX1 and that the TAL1 complex directly activates the MYB oncogene, forming a positive feed-forward regulatory loop that reinforces and stabilizes the TAL1-regulated oncogenic program. One of the critical downstream targets in this circuitry is the TRIB2 gene, which is oppositely regulated by TAL1 and E2A/HEB and is essential for the survival of T-ALL cells.

**Scientific Abstract:**

The oncogenic transcription factor TAL1/SCL is aberrantly expressed in over 40% of cases of human T cell acute lymphoblastic leukemia (T-ALL), emphasizing its importance in the molecular pathogenesis of T-ALL. Here we identify the core transcriptional regulatory circuit controlled by TAL1 and its regulatory partners HEB, E2A, LMO1/2, GATA3, and RUNX1. We show that TAL1 forms a positive interconnected autoregulatory loop with GATA3 and RUNX1 and that the TAL1 complex directly activates the MYB oncogene, forming a positive feed-forward regulatory loop that reinforces and stabilizes the TAL1-regulated oncogenic program. One of the critical downstream targets in this circuitry is the TRIB2 gene, which is oppositely regulated by TAL1 and E2A/HEB and is essential for the survival of T-ALL cells.

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